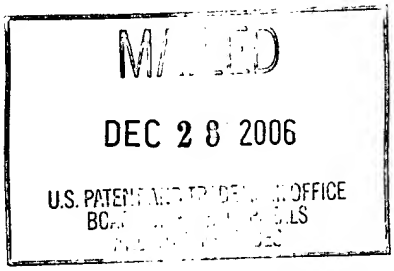
The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DENISA D. WAGNER, and ROBERT C. JOHNSON



Appeal No. 2006-3088
Application No. 08/948,393

ON BRIEF

Before MILLS, LINCK, and LEBOVITZ, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 71, 81, 85, 87-89, 92, and 94-97.

Claims 71 reads as follows:

> 71. A method for treating or inhibiting atherosclerosis by decreasing the formation or growth of plaque on arterial walls in a mammal comprising:
> providing an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin, said P-selectin being on an endothelial cell; and
> administering said agent to mammal in need of such treatment so as to cause such inhibition to occur, said agent being administered repeatedly in sequential doses or by the controlled release to the mammal over a period of months or years,
> wherein said agent is selected from the group consisting of PSGL-1, soluble forms of PSGL-1, fragments of PSGL-1, and mimetics of PSGL-1 which

resemble PSGL-1 in shape and charge distribution, said agent being effective to inhibit the interaction between P-selectin and a ligand of P-selectin and between E-selectin and a ligand of E-selectin.

The prior art cited by the examiner is:

Aberg et al. (Aberg)	5,061,694	Oct. 29, 1991
Casscells et al. (Casscells)	5,308,622	May 3, 1994
Cummings et al. (Cummings)	5,464,778	Nov. 7, 1995
Larsen et al. (Larsen)	5,840,679	Nov. 24, 1998
Tedder et al. (Tedder)	5,834,425	Nov. 10, 1998
Coller et al. (Coller)	5,976,532	Nov. 2, 1999

De Felice et al. (De Felice), "Current Therapy of Peripheral Obstructive Arterial Disease. The Non-Surgical Approach," Angiology -The Journal of Vascular Diseases, Vol. 41, No. 1, pp. 1-11 (1990)

Hinstridge et al. (Hinstridge), "An Overview of Therapeutic Interventions in Myocardial Infarction Emphasis on Secondary Prevention," Drugs, Vol. 42, (Suppl 2): pp. 8-2 (1991)

The Merck Manual of Diagnostics and Therapy, Sixteenth Ed., edited by Berkow et al., Merck Research Laboratories, Rahway, NJ, pp. 409-413 (1992)

Sluiter et al., (Sluiter), "Leukocyte Adhesion Molecules on the Vascular Endothelium: Their Role in the Pathogenesis of Cardiovascular Disease and the Mechanisms Underlying their Expression," Journal of Cardiovascular Pharmacology, Vol. 22, (Suppl. 4), pp. S37-S44 (1993)

Grounds of Rejection

Claims 71, 81, 85, 87-89, 92, and 94-97 stand rejected under 35 U.S.C. § 103(a) over Cummings in view of Larsen, Tedder, Coller, and Sluiter in further view of Aberg, Casscells, and Hinstridge, in view of the Merck Manual.

We affirm the obviousness rejection before us.

Claim Grouping

Appellants argue claims 71, 81, 85, 87-89, 92, and 94-97 as a single group with respect to each. Brief, page 6. Therefore, we select claim 71, as representative of the rejected claims. 37 CFR § 41.37(c)(1)(vii) (September 13, 2004).

DISCUSSION

35 U.S.C. § 103

Claims 71, 81, 85, 87-89, 92, and 94-97 stand rejected under 35 U.S.C. § 103(a) over Cummings in view of Larsen, Tedder, Coller, and Sluiter in further view of Aberg, Casscells, and Hinstridge, in view of the Merck Manual.

To begin, the examiner states for the record that PSGL taught by Cummings and Larsen is the same PSGL-1 as that claimed, and indicates there has been no dispute regarding this matter in the prosecution of the application. Answer, page 5.

The examiner contends Cummings teaches the use of PSGL in the treatment of leukocyte adherence, inflammation and coagulation including ischemia-reperfusion

injury and atherosclerosis. Answer, page 5. Cummings further teaches the properties and use of PSGL, including protein fragments thereof, as well as its administration to treat pathological conditions including atherosclerosis. Id. Cummings teaches that platelet leukocyte interactions are believed to be important in atherosclerosis (column 19, lines 64-67) and that pathological situations in which leukocytes cause tissue damage include atherosclerosis (column 18, lines 54-62).

The examiner finds, however, that Cummings differs from the claimed invention by not disclosing "said agent being administered repeatedly in sequential doses or by the controlled release to the mammal over a period of months or years" as required by claim 71. Id., at 6. The examiner notes that Cummings does not disclose treating or inhibiting "atherosclerosis by decreasing the formation or growth of plaque on arterial walls" and further does not disclose the various art recognized "vessel-corrective techniques" or dosages. Id., at 6.

The examiner relies on Aberg for its teaching that slowing the progress of atherosclerosis, includes the reduction or elimination of atherosclerotic lesions, and its teaching that sustained release formulations for the treatment of atherosclerosis may be administered biweekly, weekly, or monthly for a period of at least one to two weeks. Answer, page 10. The examiner further indicates that Appellants amendment of the claims to recite that the claimed treatment method works "by decreasing the formation or growth of plaque on arterial walls," simply amends the claims to recite underlying characteristics of the same therapeutic endpoint of treating atherosclerosis. Answer,

The examiner concludes that, "given the long term chronic nature of atherosclerosis, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide prolonged treatment of an appropriate inhibitor to meet the needs of the patient and the particular state of the disease, which has been standard practice by the medical profession." Answer, page 10.

The additional cited references appear to be cumulative to the disclosures of Cummings and Aberg. For example, Larsen is also cited for the teaching that PGSL, including its fragments, can treat conditions characterized by P- or E-selectin mediated intracellular adhesion (Answer, page 6). Tedder is cited as evidence that it is known in the art to generate and use chimeric peptides by combining the ligand binding portions, including those derived from P-selectin (Answer, page 7). Coller is cited to show art known vessel-corrective techniques in the treatment of cardiovascular disorders such as atherosclerosis. Id. Sluiter is additional evidence that one of ordinary skill in the art would have targeted the inhibition of P-selectin-mediated events in therapeutics of inhibiting leukocyte adhesion to alleviate tissue damage in cardiovascular disease (Answer, page 8). Merck describes the pathogenosis of atherosclerosis as involving a chronic endothelial injury hypothesis associated with platelets, monocytes and associated growth factors (Answer, page 9). De Felice is relied on for its disclosure that it is known that mural thrombi contribute to the development and progression of atherosclerotic plaque. Id. Casscells teaches that atherosclerosis results from the

development of an intimal lesion, and that treatment over a period of time is preferred. Id.

The examiner concludes that the cumulative references as a whole would have rendered the claimed invention obvious. Answer, page 11. We agree with the examiner's analysis and that the examiner has provided sufficient evidence to support a prima facie case of obviousness.

Where the prior art, as here, anticipates or renders obvious the claimed invention, the burden then falls on an appellants to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990).

In response to the examiner's prima facie case of obviousness, Appellants contend that a prima facie case of obviousness in view of Cummings and the other cited references has not been established because Cummings is not prior art to the present application because it has been antedated by a Declaration of record under 37 CFR § 1.131. Brief, page 5.

37 CFR § 1.131 states in relevant part:

> (a) When any claim of an application or a patent under reexamination is rejected, the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based. The effective date of a U.S. patent, U.S. patent application publication, or international application publication under PCT Article 21(2) is the earlier

> of its publication date or date that it is effective as a reference under 35 U.S.C. 102(e). Prior invention may not be established under this section in any country other than the United States, a NAFTA country, or a WTO member country. Prior invention may not be established under this section before December 8, 1993, in a NAFTA country other than the United States, or before January 1, 1996, in a WTO member country other than a NAFTA country. Prior invention may not be established under this section if either:
>
> . . .
>
> (b) The showing of facts shall be such, in character and weight, as to establish reduction to practice prior to the effective date of the reference, or conception of the invention prior to the effective date of the reference coupled with due diligence from prior to said date to a subsequent reduction to practice or to the filing of the application. Original exhibits of drawings or records, or photocopies thereof, must accompany and form part of the affidavit or declaration or their absence must be satisfactorily explained.
>
> Moreover, a 37 CFR § 131 affidavit or declaration showing must
>
> establish possession of the invention (i.e., the basic inventive concept) and not just of what one reference (in a combination of applied references) happens to show, if that reference does not itself teach the basic inventive concept. In re Spiller, 500 F.2d 1170, 182 USPQ 614 (CCPA 1974).
>
> The Manual of Patent Examining Procedure (MPEP) § 715.

The examiner did not find Appellants' Declaration under 37 CFR 1.131 persuasive. The examiner responded in detail to Appellants' Declaration under 37 CFR § 1.131 in the Office Action dated Oct. 21, 2004, page 4 as well as the Answer, pages 22-26. The examiner found that (Office Action dated Oct. 21, 2004, page 4)

> Applicant's evidence of conception and diligence does not address the critical elements of the instant claims which are drawn to a method of treating or inhibiting atherosclerosis in a mammal by administering PSGL-1.

> There is insufficient evidence that one of ordinary skill in the art would have taken applicant[s]' statement that: "Macrophages eat bits of activated platelets, ELAM1=PADGEM. Do monocytes bind to Padgem on platelets? Padgem is an opsonizing agent to get rid of debris of platelets." to establish possession of treating atherosclerosis in a mammal by administering PSGL-1.

As discussed here, we agree with the examiner that Appellants' Declaration under 37 CFR § 1.131 is insufficient to antedate the U.S. filing date of Cummings, March 8, 1989 because it does not establish conception of the claimed invention. To begin, the Declaration under 37 CFR § 1.131 fails to explain the nexus between the evidence (1988 meeting notes) relied upon to show conception of the subject matter presently claimed. For example, the Declaration evidence as of 1988 fails to discuss a method for treating or inhibiting atherosclerosis, fails to explain the relationship or process by which P-selectin acts to decrease the formation or growth of plaque on arterial walls in a mammal, and fails to relate that one of ordinary skill in the art would have understood in 1988 that P-selectin is an agent for inhibiting an interaction between P-selectin and a ligand of P-selectin, or that P-selectin is present on an endothelial cell. At least one of these understandings would appear necessary to relate the statement written on the 1988 lecture notes to conception of the subject matter of the pending claims.

In addition, Appellants' Declaration under 37 CFR § 1.131 fails to establish due diligence from the time of conception to the time of a constructive reduction to practice of the claimed invention. Where conception occurs prior to the date of the reference,

but reduction to practice is afterward, it is not enough merely to allege that applicant or patent owner had been diligent. Rather, applicant must show evidence of facts establishing diligence. Under 37 CFR § 1.131, the critical period in which diligence must be shown begins just prior to the effective date of the reference or activity and ends with the date of a reduction to practice, either actual or constructive (i.e., filing a United States patent application). See, Ex parte Merz, 75 USPQ 296, 297 (Bd. App. 1947).

Appellants further allege an actual reduction to practice as early as May 6, 1994 (Declaration, paragraph 9), and a reduction to practice of a mouse model on Sept 13, 1993 (Declaration, paragraph 7) all of which occurred after the Nov. 16, 1992 filing date of Cummings.[1]

Appellants' earliest application priority date serving as a constructive reduction to practice of their invention is April 28, 2000 (provisional application 60/200,590). Appellants' Declaration under 37 CFR § 1.131 does not appear to factually account for the period between the 1988 meeting notes and experiments performed on February 28, 1992. If Appellants rely on their priority date as a constructive reduction to practice of their invention, Appellants' Declaration does not account for the period between May 6, 1994 and the filing of the provisional patent application on April 28, 2000. An Applicant may be diligent within the meaning of the patent law when he or she is doing nothing, if his or her lack of activity is excused. Note, however, that the record must set forth an explanation or excuse for the inactivity; the USPTO or courts will not speculate

1 Cummings is a C-I-P of applications having an even earlier filing date.

on possible explanations for delay or inactivity. See In re Nelson, 420 F.2d 1079, 164 USPQ 458 (CCPA 1970).

Thus, for the reasons herein, we conclude Appellants' Declaration under 37 CFR § 1.131 is insufficient to overcome the prior art rejection of the claims for obviousness over Cummings, and the other cited references.

Appellants also argue that Cummings does not teach or suggest that the reference contemplates the use of PSGL-1 for reducing the formation of arterial plaque. Rather, Cummings directs one skilled in the art to treat thrombus (blood clot) formation. Brief, page 5. The examiner responds to this argument, asserting that Cummings clearly teaches treating atherosclerosis and long term treatment with PSGL. Answer, page 12. See also, Cummings, column 18, lines 51 and 62, Column 19, line 64 to Column 20, line 5.

Similarly, Appellants argue that the Declaration under 37 CFR § 1.132 of Wagner, paragraphs 5 and 6, indicates that Cummings "is directed to prevention of platelet activation in the circulatory system, rather that [sic] the inhibition of endothelial cell binding which is an essential component of atherosclerosis." Brief, page 5.

The examiner directs Appellants' attention to Cummings, Column 18, lines 34-62 which state that,

> [s]ince P-selectin has several functions related to leukocyte adherence, inflammation, tumor metastasis and coagulation, clinically, compounds which interfere with binding of P-selectin and/or other selectins, including E-selectin and L-selectin, . . . can be used to modulate these responses. . . . For example, the glycoprotein ligand or components thereof can . . . be used to inhibit leukocyte adhesion by competitively binding to P-

> selectin expressed on the surface of activated platelets or endothelial cells.

Thus, in contrast to the statements in the Wagner Declaration under 37 CFR § 1.132 put forth by Appellants, it is evident that Cummings recognized that P-selectin was expressed on the surface of platelets and endothelial cells, and that inhibitors of P-selectin could be used to inhibit leukocyte adhesion. Cummings also recognized the role of platelet-leukocyte interactions in atherosclerosis. Col. 19, lines 64-47. The additional cited references, including Aberg, also establish that atherosclerosis is associated with plaque formation and is a chronic condition requiring long term treatment such as daily, weekly or monthly dosages.

Appellants acknowledge that they do not claim to have discovered the scientific basis of atherosclerosis. Brief, page 6. The examiner has cited Merck and DeFelice for this teaching. Brief, page 6. Appellants argue that neither Aberg, Casscells, or Hinstridge "relate[s] to the use of appellant's agent for the treatment of diseases" and that it is "entirely speculative to suggest that the use of appellants' particular agents for the treatment of atherosclerosis can be administered over a long period of time and that such treatment would have beneficial results." Id.

However, non-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references. In re Merck & Co., Inc., 800 F.2d 1091, 1097, 231 USPQ 375, 380 (Fed. Cir. 1986). The test of obviousness is "whether the teachings of the prior art, taken as

a whole, would have made obvious the claimed invention." In re Gorman, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed. Cir. 1991). For the reasons discussed in detail above, we conclude that the combined teachings of the cited references would have rendered obvious the claimed invention.

In view of the above, we do not find that Appellants have convincingly rebutted the examiner's prima facie case of obviousness and the rejection of the claims for obviousness is affirmed.

CONCLUSION

The rejection of the claims 71, 81, 85, 87-89, 92, and 94-97 under 35 U.S.C. § 103(a) over Cummings in view of Larsen, Tedder, Coller, and Sluiter in further view of Aberg, Casscells, and Hinstridge, in view of the Merck Manual is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Demetra J. Mills
Administrative Patent Judge

Richard M. Lebovitz
Administrative Patent Judge

Nancy J. Linck
Administrative Patent Judge

) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES

DJM/jlb

Gosz and Partners, LLP
450 Bedford Street
Lexington, MA 02420